

<b>Office Action Summary</b>	Application No. <b>09/255,655</b>	Applicant(s) <b>Vigh et al.</b>
	Examiner <b>Howard Owens</b>	Art Unit <b>1623</b>



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1)  Responsive to communication(s) filed on Mar 23, 2001

2a)  This action is FINAL.      2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

#### Disposition of Claims

4)  Claim(s) 1-12 is/are pending in the application.

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-12 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved.

12)  The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.

2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

15)  Notice of References Cited (PTO-892)

18)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

16)  Notice of Draftsperson's Patent Drawing Review (PTO-948)

19)  Notice of Informal Patent Application (PTO-152)

17)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

20)  Other: \_\_\_\_\_

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***Response to Supplemental Response***

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action 10 has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/25/01 has been entered.

An action on the merits of claims 1-12 is contained herein below.

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The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**35 U.S.C. § 103**

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Claims 1-12 are rejected under 35 U.S.C. § 103 as being unpatentable over Zehner, U.S. Patent No. 4,786,722, in combination with Morelli, U.S. Patent No. 5,709,857, MacFarlane et al., *The Large Intestine: Physiology, Pathophysiology and Disease*, pp. 51-92, 1991 and Mortensen et al., *American Institute of Nutrition*, pp. 321-325, for the reasons of record recited below.

Claims 1-6 are drawn to a method for inducing production of butyrate comprising administering D-tagatose.

Claims 7-12 are drawn to a method for stimulating the growth of lactobacilli and lactic acid bacteria comprising administering D-tagatose.

MacFarlane et al. teach that bacterial populations such as Lactobacilli grow on carbon sources supplied by substrates such as monosaccharides and disaccharides(pp. 52-56). MacFarlane et al. also teach that unabsorbed sugars and

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alcohols are substrates available for fermentation in the human colon wherein the byproducts are SCFA's such as butyrate and propionate(see table 4).

Mortensen et al. teach that a substantial capacity for enhancement of the Short Chain Fatty Acid (propionate and butyrate specifically) production is available when sufficient amounts of an appropriate substrate are present (p. 324, paragraphs 2) that substrate being monosaccharides such as hexoses, pentoses or uronic acid monomers (p. 322, lines 1-9). However, Mortensen does not specifically cite D-tagatose.

Zehner teaches that D-tagatose is slowly degraded by indigenous microflora such as *Lactobacillus casei* and is metabolized at a small extent by the body. Zehner also teaches that D-tagatose may serve as a bulking agent in foodstuffs, juices or other liquid preparations(col.2-col.3).

Morelli teaches that several species of *Lactobacillus* positively ferment carbohydrates such as Tagatose, see tables 3 and 4.

Mortensen et al. and Macfarlane et al. teach the production of butyrate from monosaccharide and disaccharide substrates broadly in the human colon, which differs from the instantly claimed invention only with respect to the fact that D-tagatose is not specifically cited; however, Zehner teaches that unabsorbable sugars such as D-tagatose are subject to fermentation in the human colon, which adequately bridges the nexus between the differences in the prior art and the invention as claimed.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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A *prima facie* case of obviousness is supported when the prior art alone would have appeared to suggest doing, at the time the invention was made, what the applicant has done.

The prior art cited supra has set forth that monosaccharides such as D-tagatose serve as a substrate for the production of Short Chain Fatty Acids such as butyrate and also allow for the growth of commensalistic indigenous flora such as Lactobacilli. Therefore, it would have been *prima facie* obvious to use D-tagatose or any other saccharide which may be positively fermented by indigenous microflora of the human large intestine in a method for inducing production of butyrate or stimulating the growth of lactobacilli and lactic acid bacteria.

One of skill in the art would have been motivated to use D-tagatose as a substrate for inducing production of butyrate or stimulating the growth of lactobacilli and lactic acid bacteria as the prior art teaches that D-tagatose is not broken down until it traverses to the large intestine, enabling the growth of positive flora such as Lactobacilli and also allowing for the production of SCFA's, specifically butyrate. Moreover, one of skill in the art would have a reasonable expectation of success for the production of butyrate or the growth of Lactobacilli with not only D-tagatose, but any other mono or disaccharide which escapes digestion in the small intestine and has been indicated by the prior art as a substrate for commensalistic flora from which SCFA's such as butyrate are produced.

Applicant's arguments filed 3/23/01 in response to the rejection of claims 1-12 under 35 U.S.C. 103(a), have been fully considered but they are not persuasive.

Applicant asserts that "while it may be generally recognized in the prior art that monosaccharides and ketohexoses may serve as substrate for the production of SCFAs and have been associated with the growth of certain bacteria, that is not the claimed invention". As cited supra, the claims of the instant invention are a method for inducing production of butyrate comprising administering D-tagatose and a method for stimulating the growth of lactobacilli and lactic acid bacteria comprising administering

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D-tagatose. D-tagatose is a monosaccharide and applicant's invention is clearly drawn to the use of a member of a class of compounds that has been recognized by the prior art to produce SCFAs and promote the growth of certain commensalistic bacteria, thus the acknowledged teachings of the prior art are probative to establishing a case of obviouness.

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Applicant continues to argue that there is nothing in the prior art relied on by the Examiner that shows or suggests that a person of ordinary skill in the art would recognize or appreciate that D-tagatose will "selectively" induce butyrate production and "selectively" stimulate the growth of Lactobacilli and lactic acid bacteria in the human colon; moreover, that this "selective" production of butyrate was only gleaned from applicant's disclosure. However, as cited previously, with regards to the "selective" production of butyrate, the prior art (Mortensen et al. and Macfarlane et al) has set forth that monosaccharides or ketohexoses serve as a substrate for the production of Short Chain Fatty Acids such as butyrate and also allow for the growth of commensalistic indigenous flora such as Lactobacilli. Mortensen et al. teaches that a substantial capacity for enhancement of the Short Chain Fatty Acid (propionate and butyrate specifically) production is available when sufficient amounts of an appropriate substrate are present (p. 324, paragraphs 2); therefore, D-tagatose is not alone in the production of butyrate in the human colon; moreover, Zehner clearly teaches that the state of the art has recognized the fermentation of D-tagatose by human microflora, specifically *Lactobacillus casei* (col.2, lines 56-67). Zehner also teaches that this fermentation could be beneficial if it is slow in the human gut and produces non-caloric metabolites (col. 2, line 67 - col.3, line 3).

The benefits of SCFA's such as butyrate are well known in the art of human nutrition, thus applicant's contention that one of skill in the art provided with a compound that is known to produce SCFA's such as butyrate from *Lactobacillus* microflora, specifically *L. casei*, would not have a reasonable expectation of success in

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the use of that compound to produce butyrate is not convincing and the finality of the last office action is maintained.

5 All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first  
10 action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

15 A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.  
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25 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mr. Howard Owens whose telephone number is (703) 306-4538. The examiner can normally be reached on Tuesday-Friday 9 a.m.-6:30 p.m. (EST). If attempts to reach the examiner by telephone are unsuccessful, Mr. Gary Geist (703) 308-1701, may be contacted. The fax phone number for Group 1600,  
Art Unit 1623 is (703) 308-4556 or 305-3592.

30 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

**Secure and confidential access to patent application status is now available; see**  
<http://www.uspto.gov/ebc/index.html> for more information.

35 **Applicant(s) may pay patent maintenance fees, non-filing application fees and maintain USPTO accounts through** <http://www.uspto.gov/web/offices/ac/comp/fin/clonedefault.htm>



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Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/255,655	02/23/99	VIGH	M 02405.0167

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ART UNIT	PAPER NUMBER
1623	20

DATE MAILED: 06/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks